

## WEST Search History

DATE: Thursday, December 22, 2005

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L5	L4 and (holo adj acp adj synthase or holo adj acyl carrier protein synthase)	41
<input type="checkbox"/>	L4	L3 and (modular or fungal)	506
<input type="checkbox"/>	L3	L2 and express\$	675
<input type="checkbox"/>	L2	L1 and (coli or yeast or plant)	687
<input type="checkbox"/>	L1	polyketide adj (synthase or synthetase)	860

END OF SEARCH HISTORY

## Hit List

First Hit	Clear	Generate Collection	Print	Fwd Refs	Bkwd Refs
Generate OACS					

Search Results - Record(s) 1 through 30 of 41 returned.

1. Document ID: US 20050233431 A1

Using default format because multiple data bases are involved.

L5: Entry 1 of 41

File: PGPB

Oct 20, 2005

PGPUB-DOCUMENT-NUMBER: 20050233431

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20050233431 A1

TITLE: Recombinant narbonolide polyketide synthase

PUBLICATION-DATE: October 20, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Ashley, Gary	Alameda	CA	US
Betlach, Melanie C.	San Francisco	CA	US
Betlach, Mary	San Francisco	CA	US
McDaniel, Robert	Palo Alto	CA	US
Tang, Li	Foster City	CA	US

US-CL-CURRENT: 435/196; 435/252.35, 435/471, 435/69.1, 536/23.2

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KMC](#) [Drawn D](#)

2. Document ID: US 20050191679 A1

L5: Entry 2 of 41

File: PGPB

Sep 1, 2005

PGPUB-DOCUMENT-NUMBER: 20050191679

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20050191679 A1

TITLE: Schizophytrium fatty acid synthase (FAS) and products and methods related thereto

PUBLICATION-DATE: September 1, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Metz, James G.	Longmont	CO	US
Weaver, Craig A.	Boulder	CO	US



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 5. Document ID: US 20050026244 A1

L5: Entry 5 of 41

File: PGPB

Feb 3, 2005

PGPUB-DOCUMENT-NUMBER: 20050026244

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20050026244 A1

TITLE: Recombinant narbonolide polyketide synthase

PUBLICATION-DATE: February 3, 2005

## INVENTOR- INFORMATION:

NAME	CITY	STATE	COUNTRY
Ashley, Gary	Alameda	CA	US
Betlach, Melanie C.	San Francisco	CA	US
Betlach, Mary	San Francisco	CA	US
McDaniel, Robert	Palo Alto	CA	US
Tang, Li	Foster City	CA	US

US-CL-CURRENT: 435/69.1; 435/193, 435/196, 435/252.3, 435/320.1, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Drawn D
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 6. Document ID: US 20040224394 A1

L5: Entry 6 of 41

File: PGPB

Nov 11, 2004

PGPUB-DOCUMENT-NUMBER: 20040224394

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040224394 A1

TITLE: Recombinant *Streptomyces hygroscopicus* host cells that produce 17-desmethylrapamycin

PUBLICATION-DATE: November 11, 2004

## INVENTOR- INFORMATION:

NAME	CITY	STATE	COUNTRY
Katz, Leonard	Oakland	CA	US
Liu, Lu	Redwood City	CA	US
Chung, Loleta M.	San Francesco	CA	US

US-CL-CURRENT: 435/119; 435/252.3, 540/456

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Drawn D
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 7. Document ID: US 20040185541 A1

L5: Entry 7 of 41

File: PGPB

Sep 23, 2004

PGPUB-DOCUMENT-NUMBER: 20040185541  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20040185541 A1

TITLE: Heterologous production of polyketides

PUBLICATION-DATE: September 23, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Santi, Daniel	San Francisco	CA	US
Dayem, Linda	San Anselmo	CA	US
Kealey, James	San Anselmo	CA	US

US-CL-CURRENT: 435/134; 435/233

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KWMC](#) [Drawn D](#)

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8. Document ID: US 20040087003 A1

L5: Entry 8 of 41

File: PGPB

May 6, 2004

PGPUB-DOCUMENT-NUMBER: 20040087003  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20040087003 A1

TITLE: Methods and cells for improved production of polyketides

PUBLICATION-DATE: May 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Hu, Zhihao	Castro Valley	CA	US
Hutchinson, C. Richard	San Mateo	CA	US

US-CL-CURRENT: 435/252.33; 435/252.3, 435/75

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KWMC](#) [Drawn D](#)

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9. Document ID: US 20040077058 A1

L5: Entry 9 of 41

File: PGPB

Apr 22, 2004

PGPUB-DOCUMENT-NUMBER: 20040077058  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20040077058 A1

TITLE: Recombinant polynucleotides encoding pro-geldanamycin producing polyketide

synthase and accessory proteins, and uses thereof

PUBLICATION-DATE: April 22, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Hutchinson, Richard C.	San Mateo	CA	US
Reid, Ralph C.	San Rafael	CA	US
Hu, Zhihao	Castro Valley	CA	US
Rascher, Andreas	San Francisco	CA	US
Schirmer, Andreas	Hayward	CA	US
McDaniel, Robert	Palo Alto	CA	US

US-CL-CURRENT: 435/119; 435/252.3, 536/23.2

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KWMC](#) | [Drawn D](#)

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10. Document ID: US 20040005672 A1

L5: Entry 10 of 41

File: PGPB

Jan 8, 2004

PGPUB-DOCUMENT-NUMBER: 20040005672

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040005672 A1

TITLE: Heterologous production of polyketides

PUBLICATION-DATE: January 8, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Santi, Daniel V.	San Francisco	CA	US
Khosla, Chaitan	Stanford	CA	US

US-CL-CURRENT: 435/76; 435/193, 435/254.2, 435/320.1, 435/483, 435/69.1

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KWMC](#) | [Drawn D](#)

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11. Document ID: US 20030235892 A1

L5: Entry 11 of 41

File: PGPB

Dec 25, 2003

PGPUB-DOCUMENT-NUMBER: 20030235892

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030235892 A1

TITLE: Production of polyketides

PUBLICATION-DATE: December 25, 2003

## INVENTOR- INFORMATION:

NAME	CITY	STATE	COUNTRY
Katz, Leonard	Oakland	CA	US
Revill, Peter	Oakland	CA	US

US-CL-CURRENT: 435/76; 435/193, 435/252.3, 435/320.1, 435/69.1, 536/23.2

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn D](#)

12. Document ID: US 20030162262 A1

L5: Entry 12 of 41

File: PGPB

Aug 28, 2003

PGPUB-DOCUMENT-NUMBER: 20030162262

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030162262 A1

TITLE: Recombinant narbonolide polyketide synthase

PUBLICATION-DATE: August 28, 2003

## INVENTOR- INFORMATION:

NAME	CITY	STATE	COUNTRY
Ashley, Gary	Alameda	CA	US
Betlach, Melanie C.	Burlingame	CA	US
Betlach, Mary	San Francisco	CA	US
McDaniel, Robert	Palo Alto	CA	US
Tang, Li	Foster City	CA	US

US-CL-CURRENT: 435/76; 435/193, 435/252.3, 435/320.1, 435/6, 435/69.1, 536/23.2

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn D](#)

13. Document ID: US 20030148469 A1

L5: Entry 13 of 41

File: PGPB

Aug 7, 2003

PGPUB-DOCUMENT-NUMBER: 20030148469

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030148469 A1

TITLE: Combinatorial polyketide libraries produced using a modular PKS gene cluster as scaffold

PUBLICATION-DATE: August 7, 2003

## INVENTOR- INFORMATION:

NAME	CITY	STATE	COUNTRY
Ashley, Gary	Alameda	CA	US
Betlach, Melanie C.	Burlingame	CA	US

Betlach, Mary	San Francisco	CA	US
McDaniel, Robert	Palo Alto	CA	US
Tang, Li	Foster City	CA	US

US-CL-CURRENT: 435/76, 435/193, 435/252.3, 435/320.1, 435/69.1, 536/23.2

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn D](#)

14. Document ID: US 20030138879 A1

L5: Entry 14 of 41

File: PGPB

Jul 24, 2003

PGPUB-DOCUMENT-NUMBER: 20030138879

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030138879 A1

TITLE: Phosphopantetheinyl transferases and uses thereof

PUBLICATION-DATE: July 24, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Lambalot, Ralph H.	Wrentham	MA	US
Gehring, Amy M.	Beulah	MI	US
Reid, Ralph	San Francisco	CA	US
Walsh, Christopher T.	Wellesley	MA	US

US-CL-CURRENT: 435/47, 435/131, 435/193, 435/252.3, 435/320.1, 435/43, 435/64,  
435/68.1, 435/69.1, 435/76

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn D](#)

15. Document ID: US 20030104597 A1

L5: Entry 15 of 41

File: PGPB

Jun 5, 2003

PGPUB-DOCUMENT-NUMBER: 20030104597

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030104597 A1

TITLE: Recombinant narbonolide polyketide synthase

PUBLICATION-DATE: June 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Ashley, Gary	Alameda	CA	US
Betlach, Melanie C.	San Francisco	CA	US
Betlach, Mary	San Francisco	CA	US
McDaniel, Robert	Palo Alto	CA	US

Tang, Li

Foster City

CA

US

US-CL-CURRENT: 435/193; 435/196, 435/200, 435/252.3, 435/320.1, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KM/C	Drawn D
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16. Document ID: US 20030064491 A1

L5: Entry 16 of 41

File: PGPB

Apr 3, 2003

PGPUB-DOCUMENT-NUMBER: 20030064491

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030064491 A1

TITLE: Genes and proteins involved in the biosynthesis of enediyne ring structures

PUBLICATION-DATE: April 3, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Farnet, Chris M.	Outremont	CA	
Staffa, Alfredo	Saint-Laurent	CA	
Zazopoulos, Emmanuel	Montreal	CA	

US-CL-CURRENT: 435/183; 435/320.1, 435/325, 435/69.1, 435/76, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KM/C	Drawn D
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17. Document ID: US 20030044938 A1

L5: Entry 17 of 41

File: PGPB

Mar 6, 2003

PGPUB-DOCUMENT-NUMBER: 20030044938

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030044938 A1

TITLE: Method to produce novel polyketides

PUBLICATION-DATE: March 6, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Khosla, Chaitan	Stanford	CA	US
Pieper, Rembert	Washington	DC	US
Luo, Guanglin	Madison	CT	US
Cane, David E.	Providence	RI	US
Kao, Camilla	Palo Alto	CA	US
Ashley, Gary	Alameda	CA	US

US-CL-CURRENT: 435/76; 435/200, 435/320.1, 435/325, 435/69.1, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMPC	Drawn D
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18. Document ID: US 20030027287 A1

L5: Entry 18 of 41

File: PGPB

Feb 6, 2003

PGPUB-DOCUMENT-NUMBER: 20030027287

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030027287 A1

TITLE: Recombinant oleandolide polyketide synthase

PUBLICATION-DATE: February 6, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Betlach, Mary C.	San Francisco	CA	US
Shah, Sanjay Krishnakant	Concord	CA	US
McDaniel, Robert	Palo Alto	CA	US
Tang, Li	Foster City	CA	US

US-CL-CURRENT: 435/76; 435/183, 435/320.1, 435/325, 435/69.1, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMPC	Drawn D
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19. Document ID: US 20020192767 A1

L5: Entry 19 of 41

File: PGPB

Dec 19, 2002

PGPUB-DOCUMENT-NUMBER: 20020192767

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020192767 A1

TITLE: Biosynthesis of polyketide synthase substrates

PUBLICATION-DATE: December 19, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Khosla, Chaitan	Palo Alto	CA	US
Pfeifer, Blaine	Palo Alto	CA	US

US-CL-CURRENT: 435/76; 435/119, 435/252.3, 435/252.33

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMPC	Drawn D
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20. Document ID: US 20020142401 A1

L5: Entry 20 of 41

File: PGPB

Oct 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020142401  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020142401 A1

TITLE: Isolated gene for methylmalonyl CoA epimerase and uses thereof

PUBLICATION-DATE: October 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Santi, Daniel	San Francisco	CA	US
Dayem, Linda	Belmont	CA	US
Kealey, James	San Rafael	CA	US

US-CL-CURRENT: 435/76; 435/252.3, 435/320.1

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KMC](#) [Drawn D](#)

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21. Document ID: US 20020142400 A1

L5: Entry 21 of 41

File: PGPB

Oct 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020142400  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020142400 A1

TITLE: Production of polyketides in bacteria and yeast

PUBLICATION-DATE: October 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Barr, Philip J.	Oakland	CA	US
Santi, Daniel V.	San Francisco	CA	US
Ashley, Gary W.	Alameda	CA	US
Ziermann, Rainer	San Mateo	CA	US

US-CL-CURRENT: 435/76; 435/193, 435/252.33, 435/254.2

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KMC](#) [Drawn D](#)

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22. Document ID: US 20020045220 A1

L5: Entry 22 of 41

File: PGPB

Apr 18, 2002

PGPUB-DOCUMENT-NUMBER: 20020045220  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020045220 A1

TITLE: Biosynthesis of polyketide synthase substrates

PUBLICATION-DATE: April 18, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Khosla, Chaitan	Palo Alto	CA	US
Pfeifer, Blaine	Stan Ford	CA	US

US-CL-CURRENT: 435/76; 435/252.3, 435/252.33, 536/7.1

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KWMC](#) [Drawn D](#)

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23. Document ID: US 20020002712 A1

L5: Entry 23 of 41

File: PGPB

Jan 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020002712

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020002712 A1

TITLE: Production of polyketides in plants

PUBLICATION-DATE: January 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Betlach, Mary C.	San Francisco	CA	US
Kealey, James T.	Davis	CA	US
Gutterson, Neal	Oakland	CA	US
Ralston, Ed	Pleasant Hill	CA	US

US-CL-CURRENT: 800/278; 435/419, 435/69.7, 536/23.74, 800/288, 800/298

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KWMC](#) [Drawn D](#)

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24. Document ID: US 6939691 B1

L5: Entry 24 of 41

File: USPT

Sep 6, 2005

US-PAT-NO: 6939691

DOCUMENT-IDENTIFIER: US 6939691 B1

TITLE: E. coli and Streptomyces host cells that contain MatBC genes or E. coli host cells that contain pcc genes useful for enhanced polyketide production

DATE-ISSUED: September 6, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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Khosla; Chaitan	Palo Alto	CA
Pfeifer; Blaine	Palo Alto	CA

US-CL-CURRENT: 435/76; 435/252.33, 435/252.35

**ABSTRACT:**

The use of enzymes that catalyze the production of starter and extender units for polyketides in *E. coli* and *Streptomyces* is described; these enzymes include malonyl CoA decarboxylase (MatA), malonyl CoA synthetase (MatB), and a malonate transporter (MatC) as well as propionyl CoA carboxylase (pcc). The matBC gene from *Streptomyces coelicolor*, the matABC genes from *Rhizobium trifoli*, and the pccB and accA2 from *Streptomyces coelicolor* are useful in specific embodiments of the claimed invention. These enzymes may be used to enhance the yield of polyketides that are natively produced or polyketides that are rationally designed. By using these techniques, the synthesis of a complete polyketide has been achieved in *E. coli* in the presence of a phosphopantetheinyl transferase, such as sfp from *Bacillus subtilis*. This achievement permits a host organism with desirable characteristics to be used in the production of such polyketides and to assess the results of gene shuffling.

27 Claims, 0 Drawing figures

Exemplary Claim Number: 1

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Draw](#) | [De](#)

25. Document ID: US 6927286 B1

L5: Entry 25 of 41

File: USPT

Aug 9, 2005

US-PAT-NO: 6927286

DOCUMENT-IDENTIFIER: US 6927286 B1

TITLE: Bleomycin gene cluster components and their uses

DATE-ISSUED: August 9, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shen; Ben	Davis	CA		
Du; Liangcheng	Davis	CA		
Sanchez; Cesar	Asturias			ES
Chen; Mei	Davis	CA		
Edwards; Daniel J.	Davis	CA		

US-CL-CURRENT: 536/23.2; 435/252.3, 435/252.35, 435/254.11, 435/320.1, 435/325,  
435/419, 536/23.1, 536/23.7

**ABSTRACT:**

This invention provides detailed sequence analysis and characterization of the gene cluster responsible for the synthesis of bleomycin in *Streptomyces verticillus*. The

bleomycin gene cluster provides the first hybrid polyketide synthase/nonribosomal peptide synthetase pathway and elucidation of the various modules and enzymatic domains characterizing the pathway provides convenient synthetic routes for bleomycins, bleomycin analogs, and various other polyketides.

10 Claims, 28 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 19

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KMC](#) [Draw D](#)

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26. Document ID: US 6912470 B2

L5: Entry 26 of 41

File: USPT

Jun 28, 2005

US-PAT-NO: 6912470

DOCUMENT-IDENTIFIER: US 6912470 B2

TITLE: Genes and proteins involved in the biosynthesis of enediyne ring structures

DATE-ISSUED: June 28, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Farnet; Chris M.	Outremont			CA
Staffa; Alfredo	Saint-Laurent			CA
Zazopoulos; Emmanuel	Montreal			CA

US-CL-CURRENT: 702/20; 530/350, 536/23.7

ABSTRACT:

Five protein families cooperate to form the warhead structure that characterizes enediyne compounds, both chromoprotein enediynes and non-chromoprotein enediynes. The protein families include a polyketide synthase and thioesterase protein which form a polyketide synthase catalytic complex involved in warhead formation in enediynes. Genes encoding a member of each of the five protein families are found in all enediyne biosynthetic loci. The genes and proteins may be used in genetic engineering applications to design new enediyne compounds and in methods to identify new enediyne biosynthetic loci.

14 Claims, 39 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 38

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KMC](#) [Draw D](#)

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27. Document ID: US 6902913 B2

L5: Entry 27 of 41

File: USPT

Jun 7, 2005

US-PAT-NO: 6902913

DOCUMENT-IDENTIFIER: US 6902913 B2

\*\* See image for Certificate of Correction \*\*TITLE: Recombinant narbonolide polyketide synthase

DATE-ISSUED: June 7, 2005

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Betlach; Melanie C.	Burlingame	CA		
Betlach; Mary	San Francisco	CA		
McDaniel; Robert	Palo Alto	CA		
Tang; Li	Foster City	CA		

US-CL-CURRENT: 435/72; 435/252.3, 435/252.33, 435/252.35, 435/320.1, 435/76,  
536/23.2, 536/23.7

## ABSTRACT:

Recombinant DNA compounds that encode all or a portion of the narbonolide polyketide synthase are used to express recombinant polyketide synthase genes in host cells for the production of narbonolide, narbonolide derivatives, and polyketides that are useful as antibiotics and as intermediates in the synthesis of compounds with pharmaceutical value.

18 Claims, 6 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 6

Full	Title	Citation	Front	Review	Classification	Date	Reference	<u>Sequences</u>	Attachments	Claims	KWIC	Drawn De
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 28. Document ID: US 6710189 B2

L5: Entry 28 of 41

File: USPT

Mar 23, 2004

US-PAT-NO: 6710189

DOCUMENT-IDENTIFIER: US 6710189 B2

TITLE: Method to produce novel polyketides

DATE-ISSUED: March 23, 2004

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Pieper; Rembert	Washington	DC		
Luo; Guanglin	Madison	CT		
Cane; David E.	Providence	RI		
Kao; Camilla	Palo Alto	CA		
Ashley; Gary	Alameda	CA		

US-CL-CURRENT: 549/271; 546/281.7

## ABSTRACT:

A polyketide, or an antibiotic which is obtainable from the polyketide by a method comprising treating the polyketide with a culture medium conditioned by *Saccharopolyspora erythraea*, selected from the group consisting of: ##STR1## ##STR2##

16 Claims, 5 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMPC	Drawn D
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 29. Document ID: US 6670168 B1

L5: Entry 29 of 41

File: USPT

Dec 30, 2003

US-PAT-NO: 6670168

DOCUMENT-IDENTIFIER: US 6670168 B1

TITLE: Recombinant *Streptomyces hygroscopicus* host cells that produce 17-desmethylrapamycin

DATE-ISSUED: December 30, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Katz; Leonard	Oakland	CA		
Liu; Lu	Redwood City	CA		
Chung; Loleta M.	San Francisco	CA		

US-CL-CURRENT: 435/252.35

## ABSTRACT:

Recombinant host cells that produce rapamycin analogues are constructed by deleting or modifying rapamycin biosynthetic gene cluster genes and are useful in the production of compounds used as antifungals, anticancers, immunosuppressants, and neurotrophins.

1 Claims, 2 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMPC	Drawn D
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 30. Document ID: US 6627427 B1

L5: Entry 30 of 41

File: USPT

Sep 30, 2003

US-PAT-NO: 6627427

DOCUMENT-IDENTIFIER: US 6627427 B1

TITLE: Heterologous production of 15-methyl-6-deoxyerthronolide B

DATE-ISSUED: September 30, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Katz; Leonard	Oakland	CA		
Revill; Peter	Oakland	CA		

US-CL-CURRENT: 435/252.3

## ABSTRACT:

Recombinant host cells that comprise recombinant DNA expression vectors that drive expression of a product and a precursor for biosynthesis of that product can be used to produce useful products such as polyketides in host cells that do not naturally produce the product or produce the product at low levels due to the absence of the precursor or the presence of the precursor in rate limiting amounts.

12 Claims, 20 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 20

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KMC](#) [Draw. D](#)[Clear](#) [Generate Collection](#) [Print](#) [Fwd Refs](#) [Bkwd Refs](#) [Generate OACS](#)

Terms	Documents
L4 and (holo adj acp adj synthase or holo adj acyl carrier protein synthase)	41

Display Format: [-] [Change Format](#)[Previous Page](#)[Next Page](#)[Go to Doc#](#)

## Hit List

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First Hit

Search Results - Record(s) 31 through 41 of 41 returned.

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31. Document ID: US 6579695 B1

Using default format because multiple data bases are involved.

L5: Entry 31 of 41

File: USPT

Jun 17, 2003

US-PAT-NO: 6579695

DOCUMENT-IDENTIFIER: US 6579695 B1

TITLE: Phosphopantetheinyl transferases and uses thereof

DATE-ISSUED: June 17, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lambalot; Ralph H.	Wrentham	MA		
Gehring; Amy M.	Beulah	MI		
Reid; Ralph	San Francisco	CA		
Walsh; Christopher T.	Wellesley	MA		

US-CL-CURRENT: 435/41; 435/193, 435/68.1, 435/69.1, 536/23.2, 536/23.7

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32. Document ID: US 6524841 B1

L5: Entry 32 of 41

File: USPT

Feb 25, 2003

US-PAT-NO: 6524841

DOCUMENT-IDENTIFIER: US 6524841 B1

TITLE: Recombinant megalomicin biosynthetic genes and uses thereof

DATE-ISSUED: February 25, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
McDaniel; Robert	Palo Alto	CA		
Volchegursky; Yanina	Emeryville	CA		

US-CL-CURRENT: 435/252.3; 435/252.35, 435/254.11, 435/320.1, 435/325, 435/419,  
536/23.1, 536/23.2, 536/23.7

## ABSTRACT:

Recombinant nucleic acids that encode all or a portion of the megAI gene of the megalomicin polyketide synthase (PKS) of *Micromonospora megalomicea* are used to produce recombinant PKS enzymes in host cells to make megalomicin, megalomicin derivatives, and other polyketides that are useful as antibiotics, motilides, and antiparasitics.

7 Claims, 70 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 70

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn D](#)

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33. Document ID: US 6509455 B1

L5: Entry 33 of 41

File: USPT

Jan 21, 2003

US-PAT-NO: 6509455

DOCUMENT-IDENTIFIER: US 6509455 B1

TITLE: Recombinant narbonolide polyketide synthase

DATE-ISSUED: January 21, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ashley; Gary	Alameda	CA		
Betlach; Melanie C.	Burlingame	CA		
Betlach; Mary	San Francisco	CA		
McDaniel; Robert	Palo Alto	CA		
Tang; Li	Foster City	CA		

US-CL-CURRENT: 536/23.2; 435/193, 435/320.1, 536/23.7

ABSTRACT:

Recombinant DNA compounds that encode all or a portion of the narbonolide polyketide synthase are used to express recombinant polyketide synthase genes in host cells for the production of narbonolide, narbonolide derivatives, and polyketides that are useful as antibiotics and as intermediates in the synthesis of compounds with pharmaceutical value.

2 Claims, 6 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 6

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn D](#)

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34. Document ID: US 6503741 B1

L5: Entry 34 of 41

File: USPT

Jan 7, 2003

US-PAT-NO: 6503741

DOCUMENT-IDENTIFIER: US 6503741 B1

TITLE: Polyketide synthase genes from Streptomyces venezuelae

DATE-ISSUED: January 7, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ashley; Gary	Alameda	CA		
Betlach; Melanie C.	Burlingame	CA		
Betlach; Mary	San Francisco	CA		
McDaniel; Robert	Palo Alto	CA		
Tang; Li	Foster City	CA		

US-CL-CURRENT: 435/183, 435/189, 435/193, 435/232, 435/252.33, 435/252.35,  
435/254.2, 435/320.1, 536/23.1, 536/23.2, 536/23.7

## ABSTRACT:

Combinatorial libraries of polyketides can be obtained by suitable manipulation of a host modular polyketide synthase gene cluster such as that which encodes the PKS for picromycin. The combinatorial library is useful as a source of pharmaceutically active compounds. In addition, novel polyketides and antibiotics are prepared using this method.

16 Claims, 37 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 30

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn D](#) 35. Document ID: US 6500960 B1

L5: Entry 35 of 41

File: USPT

Dec 31, 2002

US-PAT-NO: 6500960

DOCUMENT-IDENTIFIER: US 6500960 B1

TITLE: Method to produce novel polyketides

DATE-ISSUED: December 31, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Pieper; Rembert	Washington	DC		
Luo; Guanglin	Madison	CT		
Cane; David E.	Providence	RI		

Kao, Camilla

Palo Alto

CA

US-CL-CURRENT: 549/264

## ABSTRACT:

Modified PKS gene clusters which produce novel polyketides in an efficient system in a host cell or in a cell free extract are described. The novel polyketides result from the incorporation of diketides of the formula ##STR1##

wherein A is a moiety that activates the diketide, and at least one of R<sup>1</sup> and R<sup>2</sup> is a substituent other than that natively occurring in the diketide normally processed by the modified PKS cluster. The polyketides may also be glycosylated to provide antibiotics.

17 Claims, 5 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMPC	Drawn D
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 36. Document ID: US 6262340 B1

L5: Entry 36 of 41

File: USPT

Jul 17, 2001

US-PAT-NO: 6262340

DOCUMENT-IDENTIFIER: US 6262340 B1

\*\* See image for Certificate of Correction \*\*TITLE: Production of polyketides in plants

DATE-ISSUED: July 17, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Betlach, Mary C.	San Francisco	CA		
Kealey, James T.	Davis	CA		
Gutterson, Neal	Oakland	CA		
Ralston, Ed	Pleasant Hill	CA		

US-CL-CURRENT: 800/278; 435/410, 435/411, 435/419, 435/69.1, 800/281, 800/284

## ABSTRACT:

The present invention provides genetically altered plants and plant cells that have been modified to contain expression system(s) capable of expressing a functional polyketide synthase (PKS). The present invention further provides methods of producing PKS and polyketides using these plants and cells.

65 Claims, 3 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMTC	Drawn D
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37. Document ID: US 6258566 B1

L5: Entry 37 of 41

File: USPT

Jul 10, 2001

US-PAT-NO: 6258566

DOCUMENT-IDENTIFIER: US 6258566 B1

\*\* See image for Certificate of Correction \*\*

TITLE: Production of polyketides in bacteria and yeast

DATE-ISSUED: July 10, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Barr; Philip J.	Oakland	CA		
Santi; Daniel V.	San Francisco	CA		
Ashley; Gary W.	Alameda	CA		
Ziermann; Rainer	San Mateo	CA		

US-CL-CURRENT: 435/76, 435/183, 435/252.3, 435/252.33, 435/252.6, 435/254.11,  
435/254.2, 435/320.1, 435/325, 435/419

ABSTRACT:

Hybrid and novel polyketide synthases (PKSs) and polyketides are produced by use of a multiple vector system. The combinatorial possibilities offered by placing the various catalytic activities of PKS systems on separate vectors permits the construction of improved libraries of PKS and polyketides. In addition, polyketides can be produced in hosts that ordinarily do not produce polyketides by supplying, along with an expression system for the desired PKS, an expression system for holo acyl carrier protein (ACP) synthase.

17 Claims, 10 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 7

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMTC	Drawn D
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38. Document ID: US 6251636 B1

L5: Entry 38 of 41

File: USPT

Jun 26, 2001

US-PAT-NO: 6251636

DOCUMENT-IDENTIFIER: US 6251636 B1

TITLE: Recombinant oleandolide polyketide synthase

DATE-ISSUED: June 26, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Betlach; Mary C.	San Francisco	CA		
Shah; Sanjay Krishnakant	Concord	CA		
McDaniel; Robert	Palo Alto	CA		
Tang; Li	Foster City	CA		

US-CL-CURRENT: 435/76; 435/252.35, 435/254.2, 435/320.1, 435/325, 435/419,  
536/23.1, 536/23.2

ABSTRACT:

Recombinant DNA compounds that encode all or a portion of the oleandolide polyketide synthase are used to express recombinant polyketide synthase genes in host cells for the production of oleandolide, oleandolide derivatives, and polyketides that are useful as antibiotics and motilides.

22 Claims, 5 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 5

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#) [Claims](#) [KMC](#) [Drawn D](#)

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39. Document ID: US 6117659 A

L5: Entry 39 of 41

File: USPT

Sep 12, 2000

US-PAT-NO: 6117659

DOCUMENT-IDENTIFIER: US 6117659 A

TITLE: Recombinant narbonolide polyketide synthase

DATE-ISSUED: September 12, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ashley; Gary	Alameda	CA		
Betlach; Melanie C.	Burlingame	CA		
Betlach; Mary	San Francisco	CA		
McDaniel; Robert	Palo Alto	CA		
Tang; Li	Foster City	CA		

US-CL-CURRENT: 435/155; 435/132, 435/189, 435/252.3, 435/252.33, 435/252.35,  
435/320.1, 536/23.2, 536/23.7

ABSTRACT:

Recombinant DNA compounds that encode all or a portion of the narbonolide polyketide synthase are used to express recombinant polyketide synthase genes in

host cells for the production of narbonolide, narbonolide derivatives, and polyketides that are useful as antibiotics and as intermediates in the synthesis of compounds with pharmaceutical value.

11 Claims, 9 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 7

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KWMC](#) | [Drawn D](#)

40. Document ID: US 6033883 A

L5: Entry 40 of 41

File: USPT

Mar 7, 2000

US-PAT-NO: 6033883

DOCUMENT-IDENTIFIER: US 6033883 A

\*\* See image for Certificate of Correction \*\*

TITLE: Production of polyketides in bacteria and yeast

DATE-ISSUED: March 7, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Barr; Philip J.	Oakland	CA		
Santi; Daniel V.	San Francisco	CA		
Ashley; Gary W.	Alameda	CA		
Ziermann; Rainer	San Mateo	CA		

US-CL-CURRENT: 435/148; 435/252.33, 435/254.21, 435/320.1, 435/471, 435/477,  
435/483, 435/484, 435/486, 435/488, 435/69.1, 435/69.7, 536/23.2, 536/23.4,  
536/23.7

ABSTRACT:

Hybrid and novel polyketide synthases and polyketides are produced by use of a multiple vector system. The combinatorial possibilities offered by placing the various catalytic activities of PKS systems on separate vectors permits the construction of improved libraries of PKS and polyketides. In addition, polyketides can be produced in hosts that ordinarily do not produce polyketides by supplying, along with an expression system for the desired PKS, an expression system for holo ACP synthase.

58 Claims, 9 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 7

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KWMC](#) | [Drawn D](#)

41. Document ID: AU 777866 B2, WO 9827203 A1, AU 9857010 A, EP 948613 A1, US

6033883 A, NZ 336140 A, AU 734325 B, US 6258566 B1, JP 2001510993 W, AU 200165515 A, US 6399789 B1, US 20020142400 A1, US 20020192756 A1

L5: Entry 41 of 41

File: DWPI

Nov 4, 2004

DERWENT-ACC-NO: 1998-362772

DERWENT-WEEK: 200504

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TITLE: Recombinant production of poly:ketide compound(s) - using separate expression systems for a minimal poly:ketide synthase and holo acyl carrier protein synthase

INVENTOR: ASHLEY, G W; BARR, P J ; SANTI, D V ; ZIERMANN, R ; ASHLEY, G ; XUE, Q

PRIORITY-DATA: 1996US-033193P (December 18, 1996), 1997US-0989332 (December 11, 1997), 1999US-0422073 (October 21, 1999), 2001AU-0065515 (August 28, 2001), 1999US-129731P (April 16, 1999), 2000US-0548060 (April 12, 2000), 2002US-0104417 (March 22, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 777866 B2	November 4, 2004		000	C12N005/10
WO 9827203 A1	June 25, 1998	E	047	C12N015/00
AU 9857010 A	July 15, 1998		000	C12N015/00
EP 948613 A1	October 13, 1999	E	000	C12N015/00
US 6033883 A	March 7, 2000		000	C12P007/26
NZ 336140 A	February 23, 2001		000	C12N015/81
AU 734325 B	June 7, 2001		000	C12N015/00
US 6258566 B1	July 10, 2001		000	C12P019/62
JP 2001510993 W	August 7, 2001		048	C12N001/21
AU 200165515 A	October 25, 2001		000	C12N005/10
US 6399789 B1	June 4, 2002		000	C07D313/16
US 20020142400 A1	October 3, 2002		000	C12P019/62
US 20020192756 A1	December 19, 2002		000	C12P021/02

INT-CL (IPC): C07 D 313/16; C12 N 1/19; C12 N 1/21; C12 N 5/06; C12 N 5/10; C12 N 9/10; C12 N 15/00; C12 N 15/09; C12 N 15/31; C12 N 15/52; C12 N 15/54; C12 N 15/62; C12 N 15/70; C12 N 15/81; C12 N 15/90; C12 P 7/26; C12 P 19/62; C12 P 21/02; G01 N 33/15; G01 N 33/50; C12 N 1/19; C12 N 1/21; C12 R 1:19; C12 R 1:865

ABSTRACTED-PUB-NO: US 6033883A

BASIC-ABSTRACT:

A recombinant host cell is modified to contain an expression system (ES) for a minimal polyketide synthase (PKS) and an ES for a holo acyl carrier protein (ACP) synthase. The minimal PKS comprises: (a) a ketosynthase/acyl transferase (KS/AT) catalytic region, a chain-length factor (CLF) catalytic region and an ACP activity for an aromatic PKS; or (b) a KS catalytic region, an AT region, and an ACP activity for a modular or fungal PKS.

Also claimed are: (1) a recombinant host cell modified to contain either: (a) at least 2 vectors (V1 and V2), where V1 contains a first selectable marker and a

first ES and V2 contains a second selectable marker and a second ES; the ESs are effective to produce at least a minimal PKS; or (b) at least one vector and a modified chromosome, the one vector containing a first selectable marker and a first ES and the modified chromosome containing a second ES, where the ESs in combination are effective to produce at least a minimal PKS as described above; (2) a library of PKSs or synthesised polyketides which comprises a panel of individual colonies, each colony containing either (a) or (b) as in (1), where the combination of vectors or of vector(s) and modified chromosome is different in each colony; (3) a vector containing a selectable marker operable in yeast or E.coli, and an ES which comprises the coding region of at least one functional PKS catalytic activity operably linked to a promoter, adapted for expression in yeast or E.coli; and (4) a yeast or E. coli cell modified to contain a vector as in (3).

USE - The host cells are used for the production of polyketides such as macrolide antibiotics, e.g. erythromycin, spiramycin and tylosin, immunosuppressants such as rapamycin and FK506, antiparasitics such as the avermectins, antifungal agents such as amphotericin B and nystatin, anticancer agents such as daunorubicin and doxorubicin and anticholesterolemics such as mevinolin.

ADVANTAGE - The use of multiple vectors provides a more efficient way to enhance the number of combinatorial forms of PKS and polyketides that can be prepared. By supplying an ES for a compatible holo ACP synthase either on a separate vector, on one of the vectors in a multiple vector system (or on a single vector for PKS expression), or as a fusion protein with a PKS or portion, hosts such as E. coli, yeast, and other microbial systems which do not customarily synthesize polyketides can be made into convenient hosts.

ABSTRACTED-PUB-NO:

US 6258566B EQUIVALENT-ABSTRACTS:

A recombinant host cell is modified to contain an expression system (ES) for a minimal polyketide synthase (PKS) and an ES for a holo acyl carrier protein (ACP) synthase. The minimal PKS comprises: (a) a ketosynthase/acyl transferase (KS/AT) catalytic region, a chain-length factor (CLF) catalytic region and an ACP activity for an aromatic PKS; or (b) a KS catalytic region, an AT region, and an ACP activity for a modular or fungal PKS.

Also claimed are: (1) a recombinant host cell modified to contain either: (a) at least 2 vectors (V1 and V2), where V1 contains a first selectable marker and a first ES and V2 contains a second selectable marker and a second ES; the ESs are effective to produce at least a minimal PKS; or (b) at least one vector and a modified chromosome, the one vector containing a first selectable marker and a first ES and the modified chromosome containing a second ES, where the ESs in combination are effective to produce at least a minimal PKS as described above; (2) a library of PKSs or synthesised polyketides which comprises a panel of individual colonies, each colony containing either (a) or (b) as in (1), where the combination of vectors or of vector(s) and modified chromosome is different in each colony; (3) a vector containing a selectable marker operable in yeast or E.coli, and an ES which comprises the coding region of at least one functional PKS catalytic activity operably linked to a promoter, adapted for expression in yeast or E.coli; and (4) a yeast or E. coli cell modified to contain a vector as in (3).

USE - The host cells are used for the production of polyketides such as macrolide antibiotics, e.g. erythromycin, spiramycin and tylosin, immunosuppressants such as rapamycin and FK506, antiparasitics such as the avermectins, antifungal agents such as amphotericin B and nystatin, anticancer agents such as daunorubicin and doxorubicin and anticholesterolemics such as mevinolin.

ADVANTAGE - The use of multiple vectors provides a more efficient way to enhance the number of combinatorial forms of PKS and polyketides that can be prepared. By

supplying an ES for a compatible holo ACP synthase either on a separate vector, on one of the vectors in a multiple vector system (or on a single vector for PKS expression), or as a fusion protein with a PKS or portion, hosts such as E. coli, yeast, and other microbial systems which do not customarily synthesize polyketides can be made into convenient hosts.

A recombinant host cell is modified to contain an expression system (ES) for a minimal polyketide synthase (PKS) and an ES for a holo acyl carrier protein (ACP) synthase. The minimal PKS comprises: (a) a ketosynthase/acyl transferase (KS/AT) catalytic region, a chain-length factor (CLF) catalytic region and an ACP activity for an aromatic PKS; or (b) a KS catalytic region, an AT region, and an ACP activity for a modular or fungal PKS.

Also claimed are: (1) a recombinant host cell modified to contain either: (a) at least 2 vectors (V1 and V2), where V1 contains a first selectable marker and a first ES and V2 contains a second selectable marker and a second ES; the ESs are effective to produce at least a minimal PKS; or (b) at least one vector and a modified chromosome, the one vector containing a first selectable marker and a first ES and the modified chromosome containing a second ES, where the ESs in combination are effective to produce at least a minimal PKS as described above; (2) a library of PKSs or synthesised polyketides which comprises a panel of individual colonies, each colony containing either (a) or (b) as in (1), where the combination of vectors or of vector(s) and modified chromosome is different in each colony; (3) a vector containing a selectable marker operable in yeast or E.coli, and an ES which comprises the coding region of at least one functional PKS catalytic activity operably linked to a promoter, adapted for expression in yeast or E.coli; and (4) a yeast or E. coli cell modified to contain a vector as in (3).

USE - The host cells are used for the production of polyketides such as macrolide antibiotics, e.g. erythromycin, spiramycin and tylisin, immunosuppressants such as rapamycin and FK506, antiparasitics such as the avermectins, antifungal agents such as amphotericin B and nystatin, anticancer agents such as daunorubicin and doxorubicin and anticholesterolemics such as mevinolin.

ADVANTAGE - The use of multiple vectors provides a more efficient way to enhance the number of combinatorial forms of PKS and polyketides that can be prepared. By supplying an ES for a compatible holo ACP synthase either on a separate vector, on one of the vectors in a multiple vector system (or on a single vector for PKS expression), or as a fusion protein with a PKS or portion, hosts such as E. coli, yeast, and other microbial systems which do not customarily synthesize polyketides can be made into convenient hosts.

US 6399789B

NOVELTY - Expressing a polyketide or non-ribosomal peptide (I) in a host cell (II) employing a number of integrative or freely replicating recombinant vectors (III), each encoding a portion of polyketide synthase (PKS) or non-ribosomal peptide synthase (NRPS) to produce (I), comprises introducing (III) into (II) and culturing (II), such that (I) is produced.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a compound (IV) selected from the group of compounds given in the specification; and
- (2) a compound (IVa) obtainable by hydroxylation and/or glycosylation of (IV).

USE - The method is useful for producing polyketides and non-ribosomal peptides (claimed).

**ADVANTAGE** - The method is suitable for creating large libraries of polyketides, non-ribosomal proteins, and mixed polyketides. The method enables the realization of the full potential of modular PKSs and NRPSSs, and thus libraries containing a complete repertoire of (I). The method requires only the construction of a limited number of highly expressing productive single mutants that will assure adequate polyketide production when the mutants are combined.

**DESCRIPTION OF DRAWING(S)** - The figure shows the macrolactones produced by *Streptomyces lividans* strains containing assorted combinations of three plasmids, pKOS010-153, pKOS038-67 and pKOS021-30.

US20020142400A

A recombinant host cell is modified to contain an expression system (ES) for a minimal polyketide synthase (PKS) and an ES for a holo acyl carrier protein (ACP) synthase. The minimal PKS comprises: (a) a ketosynthase/acyl transferase (KS/AT) catalytic region, a chain-length factor (CLF) catalytic region and an ACP activity for an aromatic PKS; or (b) a KS catalytic region, an AT region, and an ACP activity for a modular or fungal PKS.

Also claimed are: (1) a recombinant host cell modified to contain either: (a) at least 2 vectors (V1 and V2), where V1 contains a first selectable marker and a first ES and V2 contains a second selectable marker and a second ES; the ESs are effective to produce at least a minimal PKS; or (b) at least one vector and a modified chromosome, the one vector containing a first selectable marker and a first ES and the modified chromosome containing a second ES, where the ESs in combination are effective to produce at least a minimal PKS as described above; (2) a library of PKSs or synthesised polyketides which comprises a panel of individual colonies, each colony containing either (a) or (b) as in (1), where the combination of vectors or of vector(s) and modified chromosome is different in each colony; (3) a vector containing a selectable marker operable in yeast or *E.coli*, and an ES which comprises the coding region of at least one functional PKS catalytic activity operably linked to a promoter, adapted for expression in yeast or *E.coli*; and (4) a yeast or *E. coli* cell modified to contain a vector as in (3).

**USE** - The host cells are used for the production of polyketides such as macrolide antibiotics, e.g. erythromycin, spiramycin and tylosin, immunosuppressants such as rapamycin and FK506, antiparasitics such as the avermectins, antifungal agents such as amphotericin B and nystatin, anticancer agents such as daunorubicin and doxorubicin and anticholesterolemics such as mevinolin.

**ADVANTAGE** - The use of multiple vectors provides a more efficient way to enhance the number of combinatorial forms of PKS and polyketides that can be prepared. By supplying an ES for a compatible holo ACP synthase either on a separate vector, on one of the vectors in a multiple vector system (or on a single vector for PKS expression), or as a fusion protein with a PKS or portion, hosts such as *E. coli*, yeast, and other microbial systems which do not customarily synthesize polyketides can be made into convenient hosts.

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Terms

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